

REMARKS

Claims 36-55 are pending in this application. The applicants thank the Examiner for indicating in the Office Action mailed on May 2, 2003, that claims 36-55 are allowed. This amendment corrects the outstanding formalities noted by the Examiner and places the application in condition for allowance. No new matter has been entered. This amendment is accompanied by both a replacement computer readable form and paper copy Sequence Listing.

Objections:

The Examiner objected to the specification and stated that the sequence disclosure contained in the application did not comply with the requirements for such a disclosure. In response, Applicants have amended the specification rendering this objection moot.

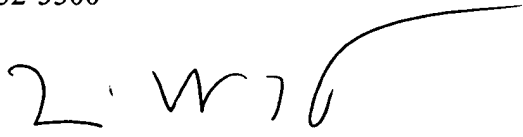
The Examiner objected to the specification stating that the first paragraph should make specific reference to earlier filed applications from which this application claims priority. In response, Applicants have amended the specification rendering this objection moot.

The applicants submit that the application is now in condition for allowance and notification to that effect is earnestly solicited.

Respectfully submitted,

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Dated: 27 June 2003

By 
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BHB/MED

MARKED-UP VERSION TO SHOW CHANGES MADE

The paragraph beginning at page 1 after the title is new.

The paragraph beginning at page 19, line 31 was replaced with the following new paragraph:

To date only twenty or so of at least one hundred predicted glycosyltransferases have been cloned and few of these have been studied with respect to their Golgi localization and retention signals (34). Studies using the elongation transferase N-acetylglucosaminyltransferase I (33-37), the terminal transferases $\alpha(2,6)$ sialyltransferase (24-26) and $\beta(1,4)$ galactosyltransferase (38-40) point to residues contained within the cytoplasmic tail, transmembrane and flanking stem regions as being critical for Golgi localization and retention. There are several examples of localization signals existing within cytoplasmic tail domains of proteins including the KDEL (SEQ ID NO: 15) and KKXX (SEQ ID NO: 16) motifs in proteins resident within the endoplasmic reticulum (41,42) the latter motif also having been identified in the cis Golgi resident protein ERGIC-53 (43) and a di-leucine containing peptide motif in the mannose-6-phosphate receptor which directs the receptor from the trans-Golgi network to endosomes (44). These motifs are not present within the cytoplasmic tail sequences of HT or GT or in any other reported glycosyltransferase. To date a localization signal in Golgi resident glycosyltransferases has not been identified and while there is consensus that transmembrane domains are important in Golgi localization, it is apparent that this domain is not essential for the localization of all glycosyltransferases, as shown by the study of Munro (45) where replacement of the transmembrane domain of $\alpha(2,6)$ sialyltransferase in a hybrid protein with a poly-leucine tract resulted in normal Golgi retention. Dahdal and Colley (46) also showed that sequences in the transmembrane domain were not essential to Golgi retention. This study is the first to identify sequence requirements for the localization of $\alpha(1, 2)$ fucosyltransferase and $\alpha(1,3)$ galactosyltransferase within the Golgi. It is anticipated that other glycosyltransferases will have similar localization mechanisms.

The paragraph beginning at page 20, line 33 with the following new paragraph:

A construct is made using PCR and subcloning as described in Example 1, such that amino acids #1 to #6 of the pig $\alpha(1,3)$ -galactosyltransferase (MNVKGR) (SEQ ID NO: 14) replace amino acids #1 to #5 of the pig secretor (Fig 6). Constructs are tested as described in Example 1.